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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,575	08/22/2006	Jerome B. Zeldis	9516-335-999	8560

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,575	ZELDIS ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *28-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/06/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application was filed on 08/22/2006, and is a national stage entry of PCT/US04/28742.

Claims 28-42 are pending, and examined herein on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 recites the limitation "Cl" in the formula. There is insufficient antecedent basis for this limitation in the claim. See claim 28, wherein X is H.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-30 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular compounds or agents for "second active ingredient" disclosed in the specification in the

method herein, does not reasonably provide enablement for any compounds in general having functional properties recited in the claims herein.

The recitations, "a dopamine agonist", "a monoamine oxidase inhibitor", "a catechol-O-methyltransferase inhibitor", "an acetylcholinesterase inhibitor", "an antiemetic", "an anti-inflammatory agent" are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating Parkinson disease comprising administering a compound as in claim 28, and any second active agent.

The breadth of the claims: The instant claims are deemed very broad since the broadest claim (i.e., claim 29) reads on any compounds having functional properties recited in the claims herein.

The relative skill of those in the art:/ The amount of direction or guidance presented:

The relative skill of those in the art is high with respect to administering a specific second active agent.

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California B. Eli Lilly* and Co. 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405 (emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case "a dopamine agonist", "a monoamine oxidase inhibitor", "a catechol-O-methyltransferase inhibitor", "an acetylcholinesterase inhibitor", "an antiemetic", "an anti-inflammatory agent", recited in the instant claims are purely functional distinction. Hence, this functional recitation read on any compounds that might have the recited functions. However, the specification merely provides those

particular compounds for functional compounds for the method herein (see pages 53-54 of the specification herein).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (Genera Electric Company v. Wabash Appliance Corporation et al. 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: The instant claimed invention is highly unpredictable as discussed below:

In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully describe genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California B. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members of genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the method herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, and side effects, especially serious toxicity that may be generated by drug-drug interactions when and/or after administration of the combination of any compounds of formula as in claim 28, and any second agent recited by function "a dopamine agonist", "a monoamine oxidase inhibitor", "a catechol-O-

methyltransferase inhibitor", "an acetylcholinesterase inhibitor", "an antiemetic", "an anti-inflammatory agent" which may encompass more than a thousand compounds. See text book Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the method herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

As discussed above, only those particular compound for each kind of functional compounds employed in the method herein is disclosed in the specification. Moreover, it is noted that the specification did not provide any working examples with the

combination of a compound of formula as in claim 28, and any second active ingredient recited by the functions herein in the treatment of Parkinson's disease. Thus, the evidence in the examples is not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed method herein.

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of a specific compound of formula as in claim 28, a specific second active agent for the combination treatment, pharmaceutical carrier, a dosage for each agent, the duration of treatment, route of treatment, etc. One would then need to test the combination in the model system to determine whether or not the combination is effective for treating Parkinson disease and one would need to test for side effects and toxicity. If the treatment is unsuccessful, one of skill in the art would have to modify the first combination, dosage, duration of treatment etc. duration of treatment, route of administration, etc. Even if successful, however, one of skill in the art would then need to determine the magnitude of the side effects and toxicity. One would then need to determine whether or not the magnitude of the side effects could be reduced by increasing or decreasing the dosage of one or both of the agents while retaining the functional aspect of the combination. Once the functionality to toxicity ratio was maximized, one would need to determine whether or not the combination which had been used was of sufficient benefit that it would serve as a useful conditioning combination. If not, one would need to select another agent and repeat the process until a sufficient benefit to detriment ratio had been achieved.

Therefore, in view of the ***Wands*** factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, and 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making solvates, of the claimed compound. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that

art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, !95 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims.

c) There is no working example of any solvate formed. These cannot be simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist.., the examples of the '881 patent do not produce the postulated compounds.., there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates or limit the claims accordingly.

g) The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is

their compositional extent". Thus, in the absence of experimentation, one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate.

h) The breadth of the claims includes all of the hundreds of thousands of unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28, 31-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hariri et al. (WO 2003/087333).

Hariri et al. teach the use of cytokine inhibitory drugs which encompass/same as instant claimed compounds of formula as in instant claims for modulating the differentiation of stem or progenitor cell population. Hariri et al. teach that the compounds therein can be used for treating diseases such as neurodegenerative disease, Alzheimer's disease, Parkinson's disease. See abstract; pages 29, 31, 33, 34, 37, 38; page 61, lines 14-16. It is also taught that the enantiomers of the selective cytokine inhibitory drug can be employed. See page 44, lines 19-22. The compounds therein can be administered orally. See page 64, lines 1-5, 16-18. Suitable dosage for oral administration of the compounds therein is between 0.1 mg to 300 mg per day. See page 66, lines 20-26

Hariri et al. does not explicitly teach the administration of the compounds therein for the treatment of Parkinson disease.

It would have been obvious to a person skilled in the art to use the claim designated compounds for the treatment of Parkinson because Hariri et al. teach that the compounds therein which encompass/same as instant compounds are useful for modulating the differentiation of stem or progenitor cell population, and can be employed for treating diseases which includes Parkinson disease. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to employ the

cytokine inhibitory drugs which encompass/read on instant claimed compounds with reasonable expectation of success of treating parkinson's disease.

Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hariri et al. (WO 2003/087333) as applied to claims 28, 31-42 above, in view of Huckle (US 6,297,286).

Hariri et al. is applied as discussed above.

Hariri et al. do not teach administration of second agent such as dopamine agonists, amantadine to treat Parkinson's disease.

Huckle teaches that amantadine, levodopa are used to treat Parkinson's disease (column 2, lines 52-54).

It would have been obvious to a person of skill in the art at the time of the invention to employ amantadine in combination with Selective cytokine inhibitory in the method of treating Parkinson's disease because Huckle teaches that amantadine can be used to treat Parkinson's disease. Accordingly, one of ordinary skill in the art would have been motivated to combine the selective cytokine inhibitory drug composition known to treat Parkinson's disease according to Hariri et al. with amantadine of Huckle with reasonable expectation of success of treating Parkinson's disease.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-

type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-31, 38-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-39 of copending Application No. 10/794877. Although the conflicting claims are not identical, they are not patentably distinct from each other because they substantially overlap. The claims of the instant application are drawn to specific compounds having cytokine inhibitory effects for the treatment of Parkinson. The claims of the co-pending application are drawn to a method of treating Parkinson disease using a cytokine inhibitory drug, which encompasses drugs of the instant claimed formula. The claims of the instant application are within the scope of the claims of the co-pending application. Therefore, the instant claims 28-31, and 38-42 are seen to be obvious over the claims 28-39 of Application No. 10/794877.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 7.30 am-3.30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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